IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Alice A. Jacobs et al. Art Unit : 1637
Serial No. : 09/996,056 Examiner : Kenneth R. Horlick
Filed : November 27, 2001
Title : CLINICALLY INTELLIGENT DIAGNOSTIC DEVICES AND METHODS

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

DECLARATION UNDER 37 C.F.R. § 1.132

I, Andrew B. Onderdonk Ph.D., declare as follows.

1. I am the Director of the Clinical Microbiology Laboratory at Brigham and Women's Hospital and am a Professor of Pathology at Harvard Medical School, both in Boston, Massachusetts. I am also the Editor-in-Chief of the Journal of Microbiology and am a reviewer or editor of several other journals. My curriculum vitae is attached hereto as Exhibit A.

2. I received a Ph.D. in Microbiology in 1973, and have worked in the fields of clinical microbiology and infectious diseases ever since. My major research interests include the role of human microflora in health and disease, in vivo and in vitro models of colonization and infection, and antimicrobial efficacy.

3. The assignee of the Jacobs et al. patent application captioned above ("the Jacobs application") is GeneVention L.L.C., which is now known as Intelligent Medical Devices, Inc. ("IMD"), and is located in Cambridge, MA. I have worked on a consulting basis with IMD since

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about May 2003. In particular, I have worked with IMD on various grant proposals, and have provided them with a number of anonymous patient respiratory samples that contain specific known viruses. Based on my interactions with personnel from IMD, I am familiar with IMD's symptom-specific disease diagnostic methods and kits.

4. I have reviewed the Jacobs application as well as an amended set of claims that applicants propose to file with the United States Patent & Trademark Office ("USPTO") on or after January 7, 2005 ("the proposed claims"). A copy of the proposed claims is attached as Exhibit B.

5. I understand that the USPTO has indicated that certain claims of the Jacobs application are identically described by, or obvious to one of ordinary skill in the relevant field in view of, U.S. Patent No. 6,083,763 to Balch (the "Balch patent"). To better understand this rejection, I have reviewed the Balch patent.

6. Based on my knowledge and experience, my review of the Balch patent, and my understanding of the invention in the Jacobs application as articulated in the proposed claims, I believe that the proposed claims cover an invention that is distinct from any subject matter disclosed in the Balch patent. Furthermore, I believe that the proposed claims would not have been obvious to one of skill in the medical diagnostics field in view of the Balch patent.

7. Although the Balch patent recites in passing the general notion of a diagnostic test for the cause of a defined set of symptoms (at column 5, lines 17-21), it is clear from the overall context and other portions of the text (e.g., column 34, lines 3-13) that Balch contemplates the use of an array of probes for one type of target, e.g., different infectious agents, such as various viral strains, or different genetic mutations, e.g., for cystic fibrosis, that are the cause of a specific disease. Thus, Balch describes at most a disease-specific array. Balch does not describe or suggest the use of symptom-specific array that includes different probes directed to two or

more very different types of targets that are known to cause a given medical symptom (but could be from various diseases) as recited in the proposed claims. For example, with respect to proposed claim 1, Balch does not describe or suggest an array that includes at least (i) a first probe or set of first probes directed to a first target, wherein the first target comprises one or more markers for one or more infectious agents known to cause the one or more medical symptoms; and (ii) a second probe or set of second probes directed to a second target, wherein the second target comprises one or more genetic markers of the subject or one or more biological or chemical molecules, all known to be a cause of the one or more medical symptoms. Balch simply does not describe or suggest anything other than the concept of a disease-specific array for one type of target. The Jacobs application, which covers methods of using symptom-specific arrays is a significant improvement over this simple Balch concept.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patents issued thereon.

Date: 1/7/05

Andrew B. Onderdonk, Ph.D.

10/21/2004 9:46:14 AM

CURRICULUM VITAE

Name: Andrew B. Onderdonk

Office Address: Channing Laboratory, 181 Longwood Ave., Boston MA 02115

Address: 28 Lynn Terrace, Westwood MA 02090

Place of Birth: Hartford, Connecticut

Education:

1969	B.A.	MacMurray College
1971	M.S.	Microbiology, University of Missouri
1973	Ph.D.	Microbiology, University of Missouri

Postdoctoral Training:

1973-1975	PHS Postdoctoral Fellow, Infectious Diseases Service, Department of Medicine UCLA, Los Angeles, CA

Licensure and Certification:

1988-1994	Clinical Laboratory Director, City of New York
1988	Clinical Laboratory Director, Bacteriology and Parasitology, State of New York
1991	Clinical Laboratory Director, National Certification Agency for Medical Laboratory Personnel, Washington, DC.

Academic Appointments:

1977-1981	Assistant Professor of Medicine, Tufts University, Boston, MA
1978-1981	Assistant Professor of Microbiology, Tufts University, Boston, MA
1979-1981	Assistant Professor of Veterinary Medicine, Tufts University, Boston,MA
1981-1982	Associate Professor, Dept of Comp Med, Tufts University, Boston, MA
1981-1990	Associate Professor, Microbiology, Tufts University, Boston, MA

1981-1990	Associate Professor of Veterinary Medicine, Tufts University, Boston, MA
1982-1990	Associate Professor, Pathology, Tufts University, Boston, MA
1984-1990	Lecturer, Harvard University, Boston, MA.
1990-2000	Associate Professor of Pathology, Harvard Medical School, Boston,MA
2000-present	Professor of Pathology, Harvard Medical School. Boston, MA

Hospital Appointments:

1975-1979	Scientific and Special Staff, Tufts New England Medical Center, Boston
1990-present	Staff Member, Department of Pathology, Brigham and Women's Hospital, Boston, MA
1990-present	Staff Member, Division of Infectious Diseases, Brigham and Women's Hospital, Boston, MA
1990-present	Director, Clinical Microbiology Laboratory, Brigham and Women's Hospital, Boston, MA

Other Professional Positions and Major Visiting Appointments:

1971-present	Consultant, Labline Industries, Melrose Park, IL
1975-1987	Consultant, Scott Laboratories, Fiskeville, RI
1977	Consultant, Upjohn Pharmaceuticals, Ann Arbor, MI
1979-1980	Acting Director, Veterinary Diagnostic Laboratory, Tufts University School of Veterinary Medicine, Boston, MA
1980-1989	Director, Veterinary Diagnostic Laboratory, Tufts University School of Veterinary Medicine, Boston, MA
1982	Consultant, Veterans Administration Central Office Research
1983-1997	Consultant, Tambrands Inc., Palmer, MA
1983	Consultant, Searle, Ltd., London, UK
1985	Consultant, Canadian Research Council, Toronto, Canada
1986-1988	Consultant, National Ileitis and Colitis Foundation
1987-1990	Director, Division of Laboratories, Tufts University School of Veterinary Medicine, Boston, MA
1988	Institutional Review Team, College of Life Sciences and Agriculture,University of New Hampshire, Durham, NH
1988-present	Member, Scientific Advisory Board, Alpha Beta Technology, Worcester, MA
1991-1993	Consultant, Adams Scientific, Fiskeville, RI
1992-present	Consultant, SmithKline Beecham, Parsippany, NJ
1994-present	Consultant, PML Microbiologics Inc., Tualanin, OR
1991-present	Science by Mail Scientist, Museum of Science, Boston, MA
1998-present	Consultant, Procter and Gamble, Cincinnati, OH
1997-present	Consultant, Genzyme Corporation, Cambridge, MA

1998-present Consultant, Osmetech Ltd, Crewe, England

Major Administrative Responsibilities:

1990-present Director, Clinical Microbiology Laboratory, Brigham and Women's Hospital, Boston, MA
1990-present Director, Anaerobe Research Laboratory, Channing Laboratory, Boston, MA

Major Committee Assignments:

Medical/Veterinary School:

1979-1981 Curriculum Committee, Tufts University School of Veterinary Medicine, Boston, MA
1980-1983 Admissions Committee, Tufts University School of Veterinary Medicine, Boston, MA
1985-1987 Curriculum Committee, Tufts University School of Veterinary Medicine, Boston, MA
1985-1988 Basic Science Tenure and Promotions Committee, Tufts University, Schools of Medicine, Veterinary Medicine, and Dental Medicine, Boston, MA
1985-1989 Chairman, Faculty Council, Tufts University School of Veterinary Medicine, Boston, MA
1994-1995 Member, Harvard University Committee on Microbiologic Safety/Committee for Research on Hazardous Biologic Agents (COMS/CRHBA)
1996-1998 Associate Chair COMS/CRHBA
1998-present Chair, Committee on Microbiologic Safety/Committee for Research on Hazardous Biologic Agents (COMS). This committee is charged with the responsibility for setting policy and determining the safety of research with any biologic agent or microorganism with infectious or hazardous potential for investigators, human subjects or the general public. The committee reviews each submitted protocol, determines an appropriate safety level and approves the research within the guidelines recommended. During my term as Chair of this committee, the complexity of issues facing the committee has increased dramatically. This committee was first established to deal primarily with laboratory based research using biologic agents, including recombinant organisms and vectors, as well as xenografts of tissues and cells in animal test systems. More recently, these recombinant vectors and xenografting strategies have been applied to human disease. Protocols for the use of xenotransplantation and for gene therapy in human subjects have resulted in substantial alterations in operating procedures for the committee and has led to the

establishment of two subcommittees, one for scientific review of gene therapy protocols and a second for scientific review of xenotransplantation protocols. Both subcommittees make recommendations to COMS, with the ultimate decision on safety made by COMS. In addition, I have formalized the policies used by COMS as part of a policy manual and I am in the process of seeking to clarify the role of this committee within the university research framework.

Hospital:

1991-present	Education Committee, Clinical Laboratories, Brigham and Women's Hospital
1994-present	Laboratory Utilization Committee, Brigham and Women's Hospital
1994-1997	Cost Management Learning Center, Brigham and Women's Hospital
1997-1998	Laboratory Consolidation Committee, Brigham and Women's Hospital
1998-present	Clinical Pathology resident Research Committee

Professional Society Involvement:

1973-present	Member, Society of Microbial Ecology and Disease
1988-present	Member, International Society for Anaerobic Bacteria
1973-present	Member, American Society for Microbiology
1975-present	Member, Northeast Branch, American Society for Microbiology
1976-present	Member, American Federation for Clinical Research
1977-present	Member, American Association for the Advancement of Science
1980-1989	Member, American Association of Veterinary Laboratory Diagnosticians
1981-present	Fellow, American Academy of Microbiology
1983	Co-Chairman, 8th International Symposium on Intestinal Microecology, Boston, MA
1986	Organizing Committee, International Symposium on Anaerobic Bacteria and Bacterial Infections. Monte Carlo, Monaco
1977-present	Fellow, Infectious Diseases Society of America
1990-present	Member, New York Academy of Science
1992-present	Member, The Academy of Clinical Laboratory Physicians and Scientists
1993	Chairman, Organizing Committee Society for Microbial Ecology and Disease, Boston, MA
1994-1995	Chairman, Organizing Committee for First World Congress on Anaerobic Bacteria and Bacterial Infections, San Juan, Puerto Rico
1996-1998	Chairman, Organizing Committee for 2nd World Congress on Anaerobic Bacteria and Bacterial Infections, Nice, France
1999-present	Chairman, Organizing Committee for World Congress on Anaerobic Bacteria and Bacterial Infections

Editorial Boards:

1984-93	Editorial Board, Infection and Immunity
1985-present	ad hoc Reviewer, New England Journal of Medicine
1989-93	Editorial Board, Journal of Clinical Microbiology
1989-present	ad hoc Reviewer, Journal of Infectious Diseases
1990-present	ad hoc Reviewer, Applied and Environmental Microbiology
1990-present	ad hoc Reviewer, Gastroenterology
1990	Guest Editor, Reviews of Infectious Diseases Supplement,
1993-99	Editor, Journal of Clinical Microbiology
1994-present	Editorial Board, Anaerobe
1998-99	Editorial Board, Clinical Microbiology Reviews
1999-present	Editor-in-Chief, Journal of Clinical Microbiology

Awards and Honors:

1973	Who's Who Among Students in American Universities and Colleges
1973	Co-Chairman, Advisory Board to the President of the University of Missouri
1973	Member, Selection Committee Dean of Student Affairs, University of Missouri
1976	Member, Sigma Xi
1976	Alumni Board of MacMurray College
1978	Vice President, Northeast Branch, American Society for Microbiology
1982-1984	President, Northeast Branch, American Society for Microbiology
1990-1996	Treasurer, International Society for Anaerobic Bacteria
1990-1992	President, Society for Microbial Ecology and Disease
1997-present	President, International Society for Anaerobic Bacteria
1999	Distinguished Alumni Award, MacMurray College

Report of Research:

Major research interests:

1. Role of human microflora in health and disease
2. Pathogenesis of obligate anaerobes
3. In vivo and in vitro models of colonization and infection
4. Antimicrobial efficacy
5. Immunomodulators as anti-infective agents

Narrative description of research:

My research encompasses several areas related to human microbial flora and its role in health and disease. My interests include the pathogenesis of obligately anaerobic microorganisms, the in vivo and in vitro modeling of both normal microflora and pathogenic microorganisms, and the evaluation and development of new therapeutic agents, including antibiotics and immunomodulators.

Over twenty years ago, an animal model simulating human intraabdominal sepsis was developed in our laboratory. This model has been used to document the role of both obligate anaerobes and facultative species during the infectious process, as well as serving as a highly predictive model for antimicrobial efficacy evaluation during a mixed infection containing both obligate anaerobes and facultative bacterial species. This model system has also been used extensively to study the pathogenesis of *Bacteroides fragilis*. The primary role of this organism in abscess development was defined and its principal virulence factor, the capsular polysaccharide, was identified in collaborative studies with Dr. Dennis Kasper. Subsequent studies spanning two decades have focused on the immunologic basis for abscess development and prevention in this model system and, more recently, evaluation of the genetics of capsule production.

My interest in inflammatory bowel diseases has resulted in ongoing studies using both animal and human models for IBD. Based on my studies of the carrageenan model for ulcerative colitis, a specific microbial component of the intestinal microflora, *Bacteroides vulgatus*, was identified as being capable of provoking ulcerations in gnotobiotic animals. These early studies allowed me to develop the quantitative microbiologic techniques that have been widely used for other human microflora studies. Our studies of antibiotic associated colitis in a hamster model led to the isolation and identification of the causative agent of this toxin mediated disease, *Clostridium difficile*. Subsequent work, in collaboration with Dr. John Bartlett, resulted in the identification of the same agent as causing human disease. Studies of ileal pouch disease in humans following surgical construction of pouch reservoirs has identified bacterial overgrowth as a potentially significant factor in the development of ileal pouchitis. My recent studies have included evaluation of the intestinal microflora of the HLA-B27 transgenic rat during development of a characteristic inflammatory bowel disease. It is of interest to note that other investigators have shown the importance of *B. vulgatus* to the development of experimental IBD in other transgenic animals. My interest and research in this area is ongoing.

Based on quantitative and qualitative vaginal microflora studies conducted as part of the assessment of the role of catamenial products in toxic shock syndrome, we have developed both predictive statistical models for vaginal microflora and in vitro continuous culture models that simulate normal and abnormal conditions. These modeling techniques have been shown to be highly predictive of both normal and abnormal vaginal microflora and are currently being used to simulate the vaginal microflora in an effort to understand the role of the

various microbial species as they relate to preterm delivery, the development of bacterial vaginosis and maintenance of a healthy vaginal micro environment.

The animal models developed in this laboratory have been used to assess the therapeutic efficacy of a variety of anti-infective agents. Most recently, we have employed the model for intraabdominal sepsis to examine the role of -glucans as possible immunomodulators. A number of ongoing studies are exploring the nature of immunomodulation and protection against intraabdominal sepsis by a variety of compounds.

Research funding information:

Years	Funding source	Role	Grant Title
1975-1985	NIH	PI	Carrageenan model for experimental ulcerative colitis
1975-1989	UpJohn, Inc.	PI	Drug efficacy studies
1982-1990	NIH/NIAID	Sub-contract	*Bacteroides fragilis*: Pathogenic mechanisms and immunity
1983-1997	Tambrands, Inc.	PI	Vaginal microflora study
1986-1988	Ileitis and Colitis Foundation of America	PI	Experimental ulcerative colitis
1987-1990	Ileitis and Colitis Foundation of America	co-PI	Microflora of biopsies of inflammatory bowel disease
1988-1996	Alpha Beta Technology	PI	In vivo evaluation of the immunomodulatory properties of yeast glucans.
1988-	Roerig/Pfizer	PI	Drug efficacy studies
1989	Smith-Kline French	PI	Drug efficacy tudies
1991-1994	Ileitis and Colitis Foundation of Canada	co-PI	Ileal pouchitis biopsy study
1992-1994	NIH	co-PI	*Bacteroides* capsule mutagenesis: effect on virulence
1993-present	Smith-Kline Beecham	PI	Development of an in vivo model for human vaginal microflora during health and disease.
1995-2000	NIH	co-PI	*Bacteroides fragilis* capsules: synthesis and virulence

1995-present	Pfizer, Inc.	PI	Use of continuous culture for kill kinetics and simulation of mixed microflora
1996-present	Genzyme Corporation	PI	Biologic effects of Seprafilm and Sepragel in an animal model of intraabdominal sepsis
1998-present	Proctor and Gamble	PI	In vivo and in vitro vaginal microflora studies
1998-present	Osmetech plc	PI	Evaluation of microbial volatile fatty acid products
1999-present	NIH	PI	QuantitativeMicrobiologic Model for Preterm Delivery
2003-present	NIH	co-PI	New England Regional Center for Excellence (NERCE) for Biodefence and Emerging Infectious Disease Research

Report of Teaching:

Local Contributions:

Medical School Courses:

1990	HMS IMD Course, Instructor 20 students 8 hours preparation,14 hour course
1991	HMS Human Systems Lecturer 160 students 4 hours preparation, 45 min lecture
1992	HMS IMD Course, Instructor 20 students 8 hours preparation,14 hour course
1993	HMS Human Systems Lecturer 160 students 4 hours preparation,45 min lecture

1993	HMS IMD Course Instructor 20 students 8hours preparation,14 hour course
1994	HMS Human Systems Lecturer 160 students 4 hours preparation, 45 min lecture
1995	HMS IMD Course Instructor 20 students 8 hours preparation, 14 hour course
1995	HMS Human Systems Lecturer 160 students 4 hours preparation, 45 min lecture
1996	HMS IMD Course Instructor 20 students 8 hours preparation,14 hour course
1998-1999	HMS IMID Tutorial Tutor

Invited Teaching Presentations

1996	Anaerobic Infections Presentation, Surgical Grand Rounds 100-150 medical staff 4 hours preparation, 1 hour presentation

Advisory and Supervisory responsibilities in Clinical or Laboratory Setting

1990- present	Teaching, training and evaluation of pathology residents in Clinical Microbiology, Brigham and Women's Hospital 3-5 Residents 120 hours/year
1981- present	Responsible for the teaching, training and evaluation of 1-2 postdoctoral fellows /year in the Anaerobe Research Laboratory, 300 hours/year.

Postdoctoral Fellows Trained:

1981-1982	Michael Shapiro, M.D. , in collaboration with Dennis Kasper, M.D., current position, Department of Surgery, BIDMC, Boston, MA
1984-1985	Dori Zalesnik, M.D., in collaboration with Dennis Kasper,M.D., current position, Division of Infectious Diseases, Beth Israel Hospital, Boston, MA
1987-1988	Arnold Zedd, M.D., current position, private practice.
1988-1989	James Breeling, M.D., in collaboration with Dennis Kasper, M.D., current position, Associate Chief of Medicine, VA Medical Center, West Roxbury, MA
1988-1990	Joanne Lindenmayer, D.V.M., Medical Foundation Scholar, current position, Instructor, Tufts University School of Veterinary Medicine.
1989-1990	Annalisa Pantosti, M.D., Istituto di Superiore, Rome, 12 month training program supported by the Italian Ministry of Health, current position, Research investigator, Istituto di Superiore, Rome Italy
1991-1993	Robin Ross, Ph.D., current position, Research Associate, Department of Medicine, Brigham

	and Women's Hospital and Channing Laboratory, HMS, Boston, MA
1990-1992	Arthur O. Tzianabos, Ph.D., in collaboration with Dennis Kasper, M.D., current position; Assistant Professor, Department of Medicine , Brigham and Women's Hospital and Channing Laboratory, HMS, Boston, MA
1994-1997	Frank Gibson, Ph.D., current position; Instructor, Boston University, Boston, MA
1994-1998	Vivien Pybus, Ph.D., Current position; Instructor, Children's Hospital, Boston, MA
1998-2000	Gabrielle Schwartzenberger, M.D., Current position; staff physician, Austria
2000-2002	Tetsuya Matsumoto, M.D., Current position; assistant professor of medicine, University of Tokyo School of Medicine
2000-2004	Begonia Ruiz, PhD. Current position, Instructor Harvard Medical School
2003-2004	Hiroshige Mikamo, Current position; Associate Professor of Medicine, Gifu Medical School

Regional National or International Contributions (last 4 years only):

Invited Presentations:

1995 Models for Vaginal Microflora, San Juan, Puerto Rico. World Congress on Anaerobic Infections

1995 Animal Models for IBD. Den Haag, Holland. Falk Foundation

1995 Polysaccharide Capsule of *B. fragilis*. Madrid, Spain. Surgical Infections Conference

1996 Microbiologic Studies of Ileal Pouch Disease. Ottawa, Canada. Trends in Inflammatory Bowel Disease

1997 Experimental Models for Assessing Antibiotic Efficacy. Munich, Germany. International Congress on Immune Consequences of Trauma, Shock and Sepsis

1998 Role of Intestinal Microflora in IBD, Falk Foundation Symposium, Tbilisi, Georgia

1998 New Therapeutic Agents for Surgical Infections SEAMA Symposium, Phuket, Thailand

Professional Leadership Roles

1973 Founder and Past President: Society for Microbial Ecology and Disease

1988 Co-founder: International Society for Anaerobic Bacteria

BIBLIOGRAPHY

Original Articles:

1. Maier BR, Onderdonk AB, Baskett RC, Hentges DJ. *Shigella* indigenous flora interactions in mice. Amer J Clin Nutr 1972;25:1433-1440.

2. Rubenstein E, Onderdonk AB, Rahal JJ. Peritonsillar infection and bacteremia caused by *Fusobacterium gonodiaformans.* J Pediat 1974;85:673-675.

3. Weinstein WM, Onderdonk AB, Bartlett JG, Gorbach SL. Experimental intraabdominal abscesses in rats. Development of animal model. Infect Immun 1974;10:1250-1255.

4. Onderdonk AB, Weinstein WM, Sullivan NM, Bartlett JG, Gorbach SL. Experimental intraabdominal abscesses in rats: Quantitative bacteriology of infected animals. Infect Immun 1974;10:1256-1259.

5. Bartlett JG, Bustetter LA, Gorbach SL, Onderdonk AB. Comparative effect of tetracycline and doxycycline on the occurrence of resistant *Escherichia coli* in the fecal flora. Antimicrob Agents Chemother 1975;7:55-57.

6. Mayhew JW, Onderdonk AB, Gorbach SL. Effects of time and growth on short chain fatty acid production by *Bacteroides fragilis*. Appl Microbiol 1975;29:472-475.

7. Weinstein WM, Onderdonk AB, Bartlett JG, Louie TJ, Gorbach SL. Antimicrobial therapy of experimental intraabdominal sepsis. J Infect Dis 1975;132:282-286.

8. Gorbach SL, Mayhew JW, Bartlett JG, Thadepalli H, Onderdonk AB. Rapid diagnosis of anaerobic infections by direct gas liquid chromatography of clinical specimens. J Clin Invest 1976;57:478-484.

9. Onderdonk AB, Bartlett JG, Louie TJ, Sullivan-Sigler N, Gorbach SL. Microbial synergy in experimental intraabdominal abscess. Infect Immun 1976;13:22-26.

10. Onderdonk AB, Johnston J, Mayhew JW, Gorbach SL. Effect of dissolved oxygen and Eh on *Bacteroides fragilis* during continuous culture. Appl Environ Microbiol 1976;31:168-172.

11. Onderdonk AB, Hermos JA, Bartlett JG. The role of the intestinal microflora in experimental colitis. Am J Clin Nutr 1977;30:1819-1925.

12. Louie TJ, Onderdonk AB, Gorbach SL, Bartlett JG. Therapy for experimental intraabdominal sepsis: Comparison of four cephalosporins with clindamycin plus gentamicin. J Infect Dis 1977;135:S18-S22.

13. Bartlett JG, Onderdonk AB, Drude E, Goldstein C, Anderka M, Alpert S, McCormack WH. Quantitative microbiology of the vaginal flora. J Infect Dis 1977;132:271-277.

14. Onderdonk AB, Kasper DL, Cisneros RL, Bartlett JG. The capsular polysaccharide of *Bacteroides fragilis* as a virulence factor: Comparison of the pathogenic potential of encapsulated and unencapsulated strains. J Infect Dis 1977;136:82-89.

15. Bartlett JG, Onderdonk AB, Cisneros RL: Clindamycin-associated colitis in hamsters: Protection by vancomycin. Gastroenterology 1977;73:772-776.

16. Onderdonk AB, Polk BF, Moon NE, Goren B, Bartlett JG. Methods for quantitative vaginal flora studies. Am J Obstet Gynecol 1977;128:777-781.

17. Kasper DL, Onderdonk AB, Bartlett JG. Quantitative determination of the antibody response to capsular polysaccharide of *Bacteroides fragilis* in an animal model of intraabdominal abscess formation. J Infect Dis 1977;136:789-795.

18. Sheckman P, Onderdonk AB, Bartlett JG. Anaerobes in spontaneous peritonitis. Lancet 1977;2:1223.

19. Bartlett JG, Onderdonk AB, Cisneros RL, Kasper DL. Clindamycin-associated colitis due to a toxin producing species of clostridium in hamsters. J Infect Dis 1977;136:701-705.

20. Kasper DL, Hayes ME, Reinap BG, Craft FO, Onderdonk AB, Polk BF. Isolation and identification of encapsulated strains of *Bacteroides fragilis.* J Infect Dis 1977;136:75-81.

21. Onderdonk AB, Moon NE, Kasper DL, Bartlett JG. Adherence of *Bacteroides fragilis* in vivo. Infect Immun 1978;19:1083-1087.

22. Bartlett JG, Chang TW, Gurwith M, Gorbach SL, Onderdonk AB. Antibiotic-associated pseudomembranous colitis due to toxin-producing clostridia. N Engl J Med 1978;298:531-534.

23. Chang TW, Bartlett JG, Gorbach SL, Onderdonk AB. Clindamycin-induced enterocolitis in hamsters as a model of pseudomembranous colitis in patients. Infect Immun 1978;20:526-529.

24. Hammerschlag MR, Alpert S, Onderdonk AB, Thurston P, Drude E, McCormack WM,
Bartlett JG. Anaerobic microflora of the vaginal flora of children. Amer J Obstet Gynecol 1978;131:853-856.

25 Mansheim BJ, Onderdonk AB, Kasper DL. Immunochemical and biologic studies of the lipopolysaccharide of *Bacteroides melaninogenicus* subspecies *assacharolyticus.* J Immunol 1978;120:72-78.

26. Bartlett JG, Moon NE, Goldstein PR, Goren B, Onderdonk AB, Polk BF. Cervical and vaginal bacterial flora: Ecological niches in the female lower genital tract. Am J Obstet Gynecol 1978;130:658-662.

27. Bartlett JG, Chang TW, Onderdonk AB. Comparison of five regiments for treatment of experimental clindamycin-associated colitis. J Infect Dis 1978;138:81-86.

28. Chang TW, Onderdonk AB, Bartlett JG. Anion exchange resins in antibiotic-associated colitis. Lancet 1978;2:258-259.

29. Bartlett JG, Chang TW, Moon N, Onderdonk AB. Antibiotic-induced lethal enterocolitis in hamsters: studies with eleven agents and evidence to support the pathogenic role of toxin-producing clostridia. Am J Vet Res 1978; 39:1525-1530.

30. Onderdonk AB, Hermos JA, Dzink JL, Bartlett JG. Protective effect of metronidazole in experimental ulcerative colitis. Gastroenterology 1978;74:521-526.

31. Bartlett JG, Moon N, Chang TW, Taylor N, Onderdonk AB. Role of *Clostridium difficile* in antibiotic-associated pseudomembranous colitis. Gastroenterology 1978;75:778-782.

32. Bartlett JG, Chang TW, Onderdonk AB. Will the real Clostridium species responsible for antibiotic associated colitis please step forward? Lancet 1979;1:338.

33. Onderdonk AB, Bartlett JG. Bacteriological studies of experimental ulcerative colitis. Am J Clin Nutr 1979;32:258-265.

34. Onderdonk AB, Louie TJ, Tally FP, Bartlett JG. Activity of metronidazole against *Escherichia coli* in experimental intraabdominal sepsis. J Antimicrob Chemother 1979;5:201-210.

35. Onderdonk AB, Lowe BR, Bartlett JG. Effect of environmental stress on *Clostridium difficile* toxin levels during continuous cultivation. Appl Environ Microbiol 1979;38:637-641.

36. Kasper DL, Onderdonk AB, Crabb J, Bartlett JG. Protective efficacy of immunization with capsular antigen against experimental infection with *Bacteroides fragilis*. J Infect Dis 1979;140:724-731.

37. Joiner KA, Onderdonk AB, Gelfand JA, Bartlett JG, Gorbach SL. A quantitative model for subcutaneous abscess formation in mice. Brit J Exp Path 1980;61:97-107.

38. Zavistoski J, Dzink J, Onderdonk AB, Bartlett JG. Quantitative bacteriology of endodontic infections. Oral Surg 1980;49:171-174.

39. Joiner KA, Gelfand JA, Onderdonk AB, Bartlett JG, Gorbach SL. Host factors in the formation of abscesses. J Infect Dis 1980;142:40-49.

40. Levy S, Marshall B, Rowse-Eagle A, Onderdonk AB. Survival of *Escherichia coli* host vector systems in the mammalian intestine. Science 1980;209:391-394.

41. Onderdonk AB, Cisneros RL, Bartlett JG. *Clostridium difficile* in gnotobiotic mice. Infect Immun 1980;28:277-282.

42. Kasper DL, Onderdonk AB, Reinap GB, Lindberg AA. Variations of *Bacteroides fragilis* with in vivo passage: presence of an outer membrane associated glycan and loss of capsular antigen. J Infect Dis 1980;142:750-756.

43. Onderdonk AB, Franklin ML, Cisneros RL. Production of experimental ulcerative colitis in gnotobiotic guinea pigs with simplified microflora. Infect Immun 1981;32:277-231.

44. Onderdonk AB, Brodasky T, Bannister B. Comparative effects of clindamycin and clindamycin metabolites in the hamster model of antibiotic-associated colitis. J Antimicrob Chemother 1981;8:383-393.

45. Onderdonk AB, Marshall B, Cisneros RL, Levy S. Competition between congenic *Escherichia coli* K-12 strains in vivo. Infect Immun 1981;32:74-79.

46. Cooperstock MS, Steffen E, Yolkin R, Onderdonk AB. *Clostridium difficile* in normal infants and sudden infant death syndrome: an association with infant formula feeding. Pediatrics 1982;70:91-95.

47. Shapiro ME, Onderdonk AB, Kasper DL, Finberg RW. Cellular immunity to *Bacteroides fragilis* capsular polysaccharide. J Exp Med 1982;154:1188-1197.

48. Onderdonk AB, Markham RB, Zaleznik DF, Cisneros RL, Kasper DL. Evidence for T-cell dependent immunity to *Bacteroides fragilis* in an intraabdominal abscess model. J Clin Invest 1982;69:9-16.

49. Beaucage CM, Onderdonk AB. Evaluation of a prereduced anaerobically sterilized medium (PRAS II) for identification of anaerobic microorganisms. J Clin Microbiol 1982;16:570-572.

50. Kasper DL, Onderdonk AB. Infection with *Bacteroides fragilis*: Pathogenesis and immunoprophylaxis in an animal model. Scand J Infect Dis 1982;S31:28-33.1

51. Brown JP, McGarraugh GV, Parkinson TM, Wingard RE Jr., Onderdonk AB. A polymeric drug for treatment of inflammatory bowel disease. J Med Chem 1983 26:1300-1307.

52. Onderdonk AB, Cisneros RL, Bronson RT. Enhancement of experimental ulcerative colitis by immunization with *Bacteroides vulgatus*. Infect Immun 1983;42:783-788.

53. Cooperstock MS, Riegle L, Woodruff CW, Onderdonk AB. Influence of age, sex and diet on asymptomatic colonization of infants with *Clostridium difficile*. J Clin Microbiol 1983;17:830-833.

54. Onderdonk AB, Steeves R, Cisneros RL, Bronson RT. Adoptive transfer of immune enhancement of experimental ulcerative colitis. Infect Immun 1984;46:64-67.

55. Notarnicola SM, Zamarchi GR, Onderdonk AB. Misidentification of mucoid variants of *Staphylococcus aureus* by standard laboratory techniques. J Clin Microbiol 1985;22:459-461.

56. Onderdonk AB, Cisneros RL. Comparison of clindamycin and metronidazole for the treatment of experimental intraabdominal sepsis produced by *Bacteroides fragilis* and *Streptococcus intermedius.* Curr Ther Res 1985;38:893-898.

57. Zaleznik DF, Finberg RW, Shapiro ME, Onderdonk AB, Kasper DL. A soluble suppressor T cell factor protects against experimental intraabdominal abscesses. J Clin Invest 1985;75:1023-1027.

58. Zaleznik DF, Zhang Z, Onderdonk AB, Kasper DL. Effect of sub-inhibitory doses of clindamycin on the virulence of *Bacteroides fragilis*: Role of lipopolysaccharide. J Infect Dis 1986;154:40-46.

59. Shapiro ME, Kasper DL, Zaleznik DF, Spriggs SL, Onderdonk AB, Finberg RW. Cellular control of abscess formation: Role of T cells in the regulation of abscesses formed in response to *Bacteroides fragilis.* J Immunol 1986;137:341-346.

60. Onderdonk AB, Zamarchi G, Walsh J, Mellor R, Munoz A, Kass E. Methods for quantitative and qualitative evaluation of vaginal microflora during menses. Appl Environ Microbiol 1986;51:333-339.

61. Cisneros RL, Onderdonk AB. Single-dose prophylaxis: Efficacy for experimental intra-abdominal sepsis. Curr Ther Res 1986;39:745-752.

62. Onderdonk AB, Bronson R, Cisneros R. Comparison of *Bacteroides vulgatus* strains in the enhancement of experimental ulcerative colitis. Infect Immun 1987;55:835-836.

63. Onderdonk AB, Zamarchi G, Rodriguez M, Hirsh M, Munoz A, Kass E. Quantitative assessment of vaginal microflora during use of tampons of various compositions. Appl Environ Microbiol 1987;53:2774-2778.

64. Onderdonk AB, Zamarchi G, Rodriguez M, Hirsh M, Munoz A, Kass E. Qualitative assessment of vaginal microflora during use of tampons of various compositions. Appl Environ Microbiol 1987;53:2779-2784.

65. Onderdonk AB, Finberg R, Kasper DL, Cisneros RL. Pathogenesis of *Bacteroides fragilis* and host immune response. Microecol Ther 1988;18:285-292.

66. Cisneros RL, Onderdonk AB. Efficacy of trospectomycin for the treatment of experimental intraabdominal sepsis. Curr Ther Res 1988;43:456-462.

67. Breeling J, Kasper DL, Cisneros RL, Onderdonk AB. Outer membrane antigens of *Bacteroides vulgatus* involved with carrageenan-induced colitis in guinea pigs. Infect Immun 1988;7:1754-1759.

68. Kasper DL, Finberg RF, Crabb J, Onderdonk AB. Immune mechanisms in the prevention of intraabdominal abscess formation. Scand J Infect Dis 1989;S62:29-34.

69. Onderdonk AB, Cisneros RL, Crabb J, Finberg RF, Kasper DL. Intraperitoneal host cellular response and in vivo killing of *Bacteroides fragilis* in a bacterial containment chamber. Infect Immun 1989;57:3030-3037.

70. Lindenmayer J, Weber M, Onderdonk AB. *Borrelia burgdorferi* infection in horses. JAVMA 1989;194:1384.

71. Cisneros RL, Onderdonk AB. Efficacy of a combination of ciprofloxacin and clindamycin for the treatment of experimental intraabdominal sepsis. Curr Ther Res 1989;46: 959-965.

72. Onderdonk AB, Finberg RF, Kasper DL, Cisneros RL. Pathogenesis of *Bacteroides fragilis* and host immune response. Microecol Ther 1989;18:285-292.

73. Lindenmayer J, Weber M, Bryant J, Marquez E, Onderdonk AB. Comparison of indirect immunofluorescent antibody assay, enzyme-linked immunosorbant assay and Western immunoblot for the diagnosis of Lyme disease in the dog. J Clin Microbiol 1990;28:92-96.

74. Cisneros RL, Bawdon R, Onderdonk AB. Efficacy of ampicillin/sulbactam for the treatment of experimental intra-abdominal sepsis. Curr Ther Res 1990; 48:1021-1029.

75. Delaney ML, Cisneros RL, Onderdonk AB. Comparison of in vivo and in vitro efficacy of ceftizoxime. Clin Therapeut 1990;12:25-30.

76. Lindenmayer J, Marshall D, Onderdonk A. Dogs as sentinels for Lyme disease in Massachusetts. Am J Pub Health 1991;81:1448-1455.

77. Pantosti A, Tzianabos AO, Onderdonk AB, Kasper DL. Immunochemical characterization of two surface polysaccharides of *Bacteroides fragilis*. Infect Immun 1991;59:2075-2082.

78. Onderdonk AB, Dvorak A, Cisneros RL, McCleod RS, Antonioli D, Silen W, Blair JE,
Cullin J, Cohen Z. Microbiologic assessment of tissue biopsy samples from ileal pouch patients. J Clin Microbiol 1992;30:312-317.

79. Dvorak AM, McCleod RS, Onderdonk AB, Monahan-Earley RA, Cullen JB, Antonioli DA, Morgan E, Blair JE, Estrella P, Cisneros RL, Cohen Z, Silen W. Human gut mucosal mast cells: ultrastructural observations and anatomic variation in mast cell-nerve associations in vivo. Int Arch Allergy Immunol 1992; 98:158-168.

80. Onderdonk AB, Cisneros RL, Hinkson PL, Ostroff GR. Anti-infective effect of poly B1-6 glucotiosyl B1-3 glucopyranose (PGG) glucan in vivo. Infect Immun 1992;60:1642-147.

81. Rodewald, AK, Onderdonk AB, Warren HB, Kasper DL. Neonatal mouse model of group B Streptococcal infection. J Infect Dis 1992;166:635-639.

82. Onderdonk AB, Delaney ML, Hinkson PL, DuBois AM. Quantitative and qualitative effect of douche preparations on vaginal microflora. Obstet Gynecol 1992;80: 333-338.

83. Dvorak AM, McLeod RS, Onderdonk A, Monahan-Early RA, Cullen JB, Antonioli DA, Morgan E, Blair JE, Estrella P, Cisneros R, Silen W, Cohen Z. Ultrastructural evidence for piecemeal and anaphylactic degranulation of human gut mucosal mast cells in vivo. Int Arch Allerg Immunol 1992;99:74-83.

84. Geshnizgani AM, Onderdonk AB. Defined medium simulating genital tract secretions for growth of vaginal microflora. J Clin Microbiol 1992; 30:1323-1326.

85. Tzianabos AO, Onderdonk AB, Rosner B, Cisneros RL, Kasper DL. Structural features of polysaccharides that induce intraabdominal abscesses. Science 1993;262: 416-419.

86. Dvorak AM, Onderdonk AB, McLeod RS, Monahan-Early RA, Cullen JB, Antonioli DA, Blair JE, Morgan ES, Cisneros RL, Estrella P, Cohen Z, Silen W. Axonal necrosis of enteric autonomic nerves in continent ileal pouches: Implications for pathogenesis of Crohn's disease. Ann Surg 1993;217: 260-271.

87. Dvorak AM, Onderdonk AB, McLeod RS, Monahan-Earley RA, Antonioli DA, Cullen J, Blair JE, Cisneros RL, Letourneau L, Morgan E, Silen W, Cohen Z. Ultrastructural identification of exocytosis of granules from human gut eosinophile in vivo. Int Arch Allergy Immunol 1993;102:33-45.

88. Pantosti A, Tzianabos AO, Reinap BG, Onderdonk AB, Kasper DL. *Bacteroides fragilis* strains express multple capsular polysaccharides. J Clin Microbiol 1993; 1850-1855.

89. McCleod RS, Antonoli D, Cullen J, Dvorak A, Onderdonk A, Silen W, Blair JE, Monahan-Earley R, Cisneros R, Cohen Z. Histologic and microbiologic features of biopsy samples from patients with normal and inflamed pouches. Dis Colon Rectum 1994;37:26-31.

90. Hirschhorn LR, Trnka Y, Onderdonk A, Lee M-L, Platt R. Epidemiology of community-acquired *Clostridium difficile*-associated diarrhea. J Infect Dis 1994;169:127-133.

91. Ross RA, Lee M-L, Delaney ML, Onderdonk AB. Mixed effect models for predicting microbial interactions in the vaginal ecosystem. J Clin Microbiol 1994;32:871-875.

92. Lee M-L, Ross RA, Delaney ML, Onderdonk AB. Predicting abnormal microbial population levels in the vaginal ecosystem. Microb Ecol Health Dis 1994;7:235-240.

93. Tzianabos AO, Onderdonk AB, Zalesnik DF, Smith R, and Kasper DL. Structural characteristics of polysaccharides that induce protection against intraabdominal abscess formation. Infect Immun 1994;62:4881-4886.

94. Nelson G, Kuppermann N, Fleisher GR, Hammer BK, Thompson CM, Garcia CT, Novitsky TJ, Parsonnet J, Onderdonk A, Siber GR, Saladino RA. Recombinant endotoxin neutralizing protein improves survival from *Escherichia coli* sepsis in a rat model. Critl Care Med 1995;23:92-98.

95. Lee M-L, Ross RA, Delaney ML, Onderdonk AB. Mathematical modeling of the vaginal microflora. Microecol Ther 1995; 23:18-21.

96. Delaney ML, DuBois AM, Onderdonk AB. Qualitative and quantitative assessment of vaginal microflora following the use of cotton tampons for two or twelve hours. Microecol Ther 1995; 23:8-15

97. Ross RA, Lee M-L, Delaney ML, Onderdonk AB. Use of continuous culture growth systems for modeling vaginal microflora behaviors. Microecol Ther 1995; 23:16-17.

98. Onderdonk AB, Winkelman J, Orni-Wasserlauf R. Confirmation by chart review of cost savings from application of exclusion criteria to urine culture requests. Lab Med 1996; 27:829-832.

99. Tzianabos AO, Kasper DL, and Onderdonk AB. Structure and function of *Bacteroides fragilis* capsular polysaccharides: Relationship to induction and prevention of abscesses. Clin Infect Dis 1995; 20:S132-140.

100. Tzianabos AO, Onderdonk AB, Smith R, and Kasper DL. Structure-function relationships for polysaccharide-induced intraabdominal abscesses. Infect Immun 1994;62:3590-3593.

101. T-Lee ML, Ross RA, Onderdonk AB. Cluster analysis of vaginal microflora data. Micoecol Ther 1995; 25:324-328.

102. Ross RA, Delaney ML, Onderdonk AB. *Candida albicans* in an in-vitro model of the vaginal ecosystem. Microecol Ther 1995; 25:320-323.

103. Cisneros RL, Onderdonk AB. In vivo efficacy of a new fluoroquinolone, BAY3118, for the treatment of intraabdominal sepsis due to challenge with a mixed microbial population. Microecol Ther 1995; 25:368-369.

104. Lee M-LT, Ross RA, Onderdonk AB. Demonstration of microbial subgroups among normal vaginal microbiota data. Microbial Ecology Health Dis 1995;8:107-112.

105. Ross RA, Lee M-LT, Onderdonk AB. Effect of *Candida infection* and clotrimazole treatment on vaginal microflora. Obstet Gynecol 1995;86:925-930.

106. Bates DW, Kuperman GJ, Rittenberg E, Teich JM, Onderdonk AB, Winkelman JW, Komaroff AL, Tanisijevic M. Reminders for redundant tests: Results of a randomized controlled trial. Symp Comp Appl Med Care 1995;19: 935.

107. Tzianabos AO, Kasper DK, Cisneros RL, Smith RS, Onderdonk AB. Polysaccharide-mediated protection against abscess formation in experimental intra-abdominal sepsis. J Clin Invest 1995;96:2727-2731.

108. Pybus V, Onderdonk AB. The effect of pH on growth and succinate production by *Prevotella bivia*. Microbial Ecol Health Dis 1996; 9:19-25.

109. Gibson FC III, Tzianabos AO, Onderdonk AO. The capsular polysaccharide complex of *Bacteroides fragilis* induces cytokine production from human and murine phagocytic cells. Infect Immun 1996; 64:1065-1069.

110. Qu Z, Ling PR, Tahan SR, Sierra P, Onderdonk AB, Bistrain BR. Protein refeeding changes protein metabolism and colonic but not small intestinal morphology in protein depleted rats. Amer Inst of Nutrit 1996; 906-916.

111. Delaney ML, Onderdonk A. Evaluation of the AnaeroPack system for growth of clinically significant anaerobes. J Clin Microbiol 1997;35:558-562.

112. Pybus V, Onderdonk AB. Evidence for a commensal, symbiotic relationship between *Gardnerella vaginalis* and *Prevotella bivia* involving ammonia: Potential significance for bacterial vaginosis. J Infect Dis 1997;175:406-13.

113. Ross RA, Onderdonk AB. Activity of the antibiotic CP-99-219 (Trovafloxacin) in a mixed microflora growth system model of intraabdominal infections in humans. Infect Dis Clin Pract 1996:5:S110-S112.

114. Onderdonk AB. Efficacy of Trovafloxacin (CP-99-219), a new fluoroquinolone, in an animal model of intraabdominal sepsis. Infect Clin Pract 1996;5:S1-S3.

115. Bates DW, Kuperman GJ, Jha A, Teich JM, Orav JE, Ma'luf N, Onderdonk A, Pugatch R, Wybenga D, Winkelman J, Brennan TA, Komaroff A, Tanisijevic M. Does the computerized display of charges affect inpatient ancillary test utilization. Arch Int Med 1997;157:2501-2508.

116. Onderdonk AB. Pharmacodynamics and microbiology of Trovafloxacin in animal models of surgical infection. Am J Surg 1998;176:Suppl 6A,39S-45S.

117. Gibson FC III, Onderdonk AB, Kasper DL, Tzianabos AO. Cellular mechanisms of abscess formation by *Bacteroides fragilis*. J Immunol 1998;160:5000-06.

118. Fridkin SK, Yokoe DS, Whitney CG, Onderdonk A, Hooper DC. Epidemiology of a dominant clonal strain of vancomycin-resistant *Enterococcus faecium* at separate hospitals in Boston, Massachusetts. J Clin Microbiol 1998;36:965-970.

119. Onderdonk AB, Richardson JA, Hammer RE, Taurog JD. Correlation of Cecal Microflora of HLA-B27 Transgenic Rats with Inflammatory Bowel Disease. Infect Immun 1998;66:6022-6023.

120. Pybus V, Onderdonk AB. A commensual symbiosis between *Prevotella bivia* and *Peptostreptococcus anaerobius* involves amino acids: potential significance to the pathogenesis of bacterial vaginosis. Fems Immunol Med Microbiol 1998 (in press).

121. Bates DW, Kuperman GJ, Rittenberg E, Teich JM, Fiskio J, Ma'luf N, Onderdonk A, Wybenga D, Winkleman J, Brennan TA, Komaroff AL, Tanasijevic. A computerized intervention to reduce redundant ancillary test utilization. Am J Med 1999 (in press).

122. Comstock LE, Coyne MJ, Tzianabos AO, Pantosti A, Onderdonk AB, Kasper DL. Analysis of a capsular polysaccharide. Infect Immun 1999;67:3525-3532.

123. Lee M-L T, DuBois A, Ross RA, Onderdonk AB. Nonliear models for in vitro kill kinetics of antibiotics. J Biopharmaceutical Stat 1999;9(2):271-277.

124. Ross RA, Onderdonk AB. Production of toxic shock syndrome toxin 1 by *Staphylococcus aureus* requires both oxygen and carbon dioxide. Infec Immun 2000; 68; 5206-5209.

125. Kalka-Moll W M, Tzianabos AO, Wang Y, Carey V, Finberg R W, Onderdonk AB, Kasper DL. Effect of molecular size on the ability of zwitterionic polysaccharides to stimulate cellular immunity. J Immunol 2000; 164:719-24.6

126. Tzianabos AO, Cisneros RL, Gerskovich J, Johnson J, Miller RJ, Burns JW, Onderdonk AB. Effect of surgical adhesion reduction devices on the propagation of experimental intra-abdominal infection. Arch Surg 1999;134(11):1254-9

127. Tzianabos AO, Russell P, Onderdonk AB, Gibson III FC, Cywes C, Chan , Finburg RW, Kasper DL. IL-2 mediates protection against abscess formation in an experiemntal model of sepsis. J Immunol 1999;163:893-897.

128. Bates DW, Kuperman GJ, Rittenberg E, Teich JM, Fiskio J, Ma'luf N, Onderdonk A, Wybenga D, Winkelman J, Brennan TA, Komaroff A, Tanisijevic M. A randomized trial of a computer-based intervention to reduce utilization of redundant laboratory tests. Am J Med 1999;166:144-50.

129. Tzianabos AO, Finberg R W, Wang Y, Chan M, Onderdonk AB, Jennings HJ, Kasper DL. T cells activated by zwitterionic molecules prevent abscesses induced by pathogenic bacteria. J Biol Chem 2000; 275:6733-6740

130. Tzianabos AO, Chandraker A, Kalka-Moll W, Onderdonk AB, Stingle F, Dong V, Finberg R W, Peach R, Sayegh MH, Kasper DL. Intraabdominal abscess formation induced by bacterial pathogens requires T cells activated by the CD28/B7 T cell co-stimulatory pathway. Infect Immun 2000; 68:6550-6555

131. Ross RA, Onderdonk AB. Production of toxic shock syndrome toxin 1 by *Staphylococcus aureus* MN8 requires both oxygen and carbon dioxide. Infect Immun 2000; 68(9):5205-5209

132. Delaney ML, Onderdonk AB. for the Microbiology and Prematurity Study Group. Nugent Score Related to Vaginal Culture in Pregnant Women. Obstet Gynecol 2001; 98:79-84

133. Matsumoto T, Nieuwenhuis EES, Cisneros RL, Ruiz-Perez B, Yamaguchi K, Blumberg RS, Onderdonk AB. Protective Effect of Ethyl 1-3-(3-dimethyl aminopropyl) Urea Dihydrochloride (EDU) against Lipopolysaccharide-Induced Death in Mice. J Med Microbiol. 2004;42(4):1559-63.

134. Matsumoto T, Nieuwenhuis EES, Schleipman AR, Ruiz B, Cisneros RL, Blumberg RS, Onderdonk AB. 1-ethyl 1-3-(3-dimethyl aminopropyl) Urea Dihydrochloride (EDU) as a Novel Therapy for arthritis. Submitted

135 Warner J, Onderdonk AB. Method for Optimizing Pulse-Field Gel Electrophoresis Banding-Pattern Data. J Mol Diagn 2003;5:21-27,

136 Nieuwenhaus E ES, Matsumoto T, Exley M, Schleipman RA, Glickman J, Bailey DT, Corazza N, Colgan SP, Onderdonk AB, Blumberg RS. CD1d-dependent, macrophage mediated clearance of *Pseudomonas aeruginosa* from lung. Nat Med. 2002; 8:588-593

137 Cisneros RL, Onderdonk AB. Comparative Efficacy of BMS-284756, a new flouroquinolone, versus Established Antimicrobial Regimens for the Treatment of Experimental Intraabdominal Sepsis in Rats. Curr Thera Res 2001;62(12);862-868.

138 Onderdonk AB, Lee M-L T, Lieberman E, Delaney ML, Tuomala RE for the Microbiology and Prematurity study Group. Quantitative Microbiologic Models for Preterm Delivery. 2003 J Clin Microbiol. 41:1073-1079.

139. Onderdonk AB, Delaney ML, Ross R, Lee M-L T, Lieberman E, Tuomala RE, MAP study Group. Quantitative and Qualitative Assessment of the Vaginal Microflora During Pregnancy. Gynecol 2001; 98:79-84

140. Vardhana S, Gene MR, Onderdonk AB, Delaney ML, Tuomala RE, Norwitz E, Witkin SS, MAP Study Group. Relationship Between a Toll-like Receptor-4 (TLLR4) Gene Polymophism and Vagial Microorganisms in Pregnant Women. (Submitted)

141. Genç MR, Delaney ML, Paraskevas L-R, Tuomala RE, Norwitz E, Onderdonk AB, Witkin SS, MAP Study Group. Cytokine Responses to Vaginal Microflora and Spontaneous Preterm Delivery. (Submitted)

142. Ruiz-Perez B, Cisneros RL, Matsumoto T, Miller RJ, Vasios, G, Calias, P, Onderdonk, AB. Protection against Lethal Intra-abdominal Sepsis by 1-(3-dimethylaminopropyl)-3-ethylurea. J. Infect Dis 2003:188: 378-87.

143. Hundley AF, Onderdonk AB, Greenberg JA. Value of Routine Urine Cultuture in the Assessment of Preterm Labor. J Reproduc Med 2003; 48:853-857.

144. Hasenbein M, Cole SE, Warner J, Lambert K, Onderdonk A, McAdam AJ. Detection of Multiple Macrolide and Lincosamide Resistant Strains of Streptococcus Pyogenes from Patients in the Boston Area. J Clin Microbiol. 2004;42(4):1559-63.

145. Parsonnet J, Hansmann MA, Delaney ML, Modern PA, DuBois AM, Wieland-Alter W, Wissemann KW, Wild JE, Jones MB, Seymour JL, Onderdonk AB. Prevalence of Toxic Shock Syndrome Toxin-1 (TSST-1)-Producing *Staphylococcus aureus* and the presence of antibodies to TSST-1 in menstruating women. Submitted JID 2/2004.

146. Mikamo H, Johri AK, Paoletti LC, Madoff LC, Onderdonk AB. Adherence, Invasion and Cytochine Production by Group B Streptococcus serotype VIII strains. Infect Immun 2004`;72(8):4716-22.

147. Nguyen DP, Genç MR, Vardhana S, Babula O, Onderdonk A, Witkin SS. Ethnic Differences of polymorphism in Cytokines and Innate Immune System Genes in Pregnant Women. (in press. Ob and Gyn May 2004)

148. Genç MR, Witkin SS, Delaney ML, Paraskevas L-R, Tuomala RE, Norwitz E, Onderdonk AB. A disproportionate increase in IL-1ß over IL-1ra in the cervicovaginal secretions of pregnant women within altered vaginal microflora correlates with preterm birth. Am J Obstet Gynecolog 2004;190:1191-7.

149. Chen KT, Puopolo KM, Eichenwald EC, Onderdonk AB, Lieberman E. , No increase in rates of early neonatal sepsis by antibiotic-resistant group B *Streptococcus* in the era of intrapartum antibiotic prophylaxis.

150. Atlas R, et al. Statement on scientific publication and security. Science. 2003;299(5610):1149

151. Atlas R, et al. Statement on the consideration of biodefence and biosecurity. Nature. 2003;421(6925):771.

152. Atlas R, et al. Uncensored exchange of scientific results. Proc Natl Acad Sci U S A. 2003;100(4):1464.

153. Breuing K, Kaplan S, Liu P, Onderdonk AB, Eriksson E. Wound fluid bacterial levels exceed tissue bacterial counts in controlled porcine partial-thickness burn infections. Plast Reconstr Surg. 2003;111(2):781-8.

Proceedings of Meetings:

1. Bartlett JG, Onderdonk AB, Louie TJ, Gorbach SL. Experimental intraabdominal sepsis. Proceedings 9th International Congress of Chemotherapy; 1975 London, England

2. Onderdonk AB, Louie TJ, Bartlett JG. Carbenicillin treatment in experimental intraabdominal abscess. Proceedings 10th International Congress of Chemotherapy;1977 Zurich, Switzerland. p. 587-588.

3. Bartlett JG, Louie RJ, Gorbach SL, Kasper DI, Onderdonk AB. Comparative efficacy of three cephalosporins and cefoxitin in experimental intraabdominal sepsis. Proceedings 10th International Congress of Chemotherapy;1977 Zurich, Switzerland. p. 298-299.

4. Onderdonk AB. Microbiologic models for inflammatory bowel diseases. Falk Symposium 85, June 29-July 1; 1995, Den Haag, Netherlands

5. Onderdonk AB. Intestinal microbiota: Control and overgrowth. Falk Symposium 100 May 26-29; 1997, Freiberg, Germany.

6. Onderdonk AB, Delaney ML. Assessment of vaginal microflora during use of various catemenial products. Proceedings European Conference on Toxic Shock Syndrome, September 10-12; 1997, London, England. p. 16-17.

7. Wang SJ, Kuperman GJ, Ohno-Machado L, Sandige H, Onderdonk A, Bates DW. Using electronic data to predict the probability of bacteremia for positive blood cultures. Proc AMIA Symp. 2000;:893-7.

8. Dubois AM, Delaney ML, Onderdonk AB. Quantitative method for determining presence of anaerobic and aerobic bacteria in placenta samples. Proc 3rd World Congress on Anaerobic Bacteria and Infection. Glascow 2003:271.

9. Delaney ML, Onderdonk AB, Harlow B. Vaginal Microbiology in women with and without vulvodynia. Proc 3rd World Congress on Anaerobic Bacteria and Infection. Glascow 2003:271.

10. Cisneros RL, Onderdonk AB. Antinicrobial efficacy of Moxifloxacin during experimental intra-abdominal sepsis. Proc 3rd World Congress on Anaerobic Bacteria and Infection. Glascow 2003:265.

11. Lee MLT, Lieberman E, Tuomala R, Delaney ML, Ross R, Duboise A, Onderdonk A. A model for predicting pre-term birth.
Proc 3rd World Congress on Anaerobic Bacteria and Infection. Glascow 2003:263.

12. Ruiz-Perez B, Miller RJ, Onderdonk AB. Urea-Based compounds protect against intraabdominal sepsis by inhibiting activation of the NF-κb pathway. Proc 3rd World Congress on Anaerobic Bacteria and Infection. Glascow 2003:259.

13. Tzianabos A, Onderdonk A. Assessment of tigecycline (GAR-936) efficacy in a rat model model for intrabdominal sepsis. Proc 3rd World Congress on Anaerobic Bacteria and Infection. Glascow 2003:253.

14. Onderdonk AB, editor. Abstracts: Third World Congress on Anaerobic Bacteria and Infections. Anaerobe 2003;9:247-276.

Reviews and Educationally Relevant Publications:

1. Bartlett JG, Onderdonk AB, Louie TJ, Kasper DL, Gorbach SL. Lessons from an animal model of intraabdominal sepsis. Arch Surg 1978;113:853-857.

2. Bartlett JG, Onderdonk AB. Virulence factors of anaerobic bacteria. Rev Infect Dis 1979;1:120-122.

3. Onderdonk AB, Kasper DL, Mansheim BJ, Louie TJ, Gorbach SL, Bartlett JG. Experimental animal models for anaerobic infections Rev Infect Dis 1979;1:291-301.

4. Bartlett JG, Chang TW, Taylor NS, Onderdonk AB. Colitis induced by *Clostridium difficile*. Rev Infect Dis 1979;1:370-378.

5. Mansheim BJ, Onderdonk AB, Kasper DL. Immunochemical characterization of surface antigens of *Bacteroides melaninogenicus*. Rev Infect Dis 1979;1:263-275.

6. Kasper DL, Onderdonk AB, Polk BF, Bartlett JG. Surface antigens as virulence factors in infection with *Bacteroides fragilis*. Rev Infect Dis 1979;1:278-288.

7. Gorbach SL, Onderdonk AB. Experimental animal models and human disease. Gastroenterology 1979;76643-645.

8. Bartlett JG, Louie TJ, Gorbach SL, Onderdonk AB. Therapeutic efficacy of 29 antimicrobial regimens in experimental intraabdominal sepsis. Rev Infect Dis 1981;3:535-542.

9. Onderdonk AB, Cisneros RL, Bartlett JG. The biological and clinical significance of *Clostridium difficile*. Crit Rev Clin Lab Sci 1:161-172, 1981.

10. Onderdonk AB, Kasper DL, Shapiro ME, Finberg RW. Role of the capsular polysaccharide of *Bacteroides fragilis* in pathogenicity. Microbiol 1982;335-337.

11. Onderdonk AB. Pasteurella multocida infections. In: Bottone E. editor. Unusual Microorganisms: Gram-negative Fastidious Species. New York, Marcel Dekker; 1983. p.103-111.

12. Onderdonk AB. Role of the intestinal microflora in ulcerative colitis. In: Hentges DH editor. Human Intestinal Microflora in Health and Disease. 1983. p.491-493.

13. Onderdonk AB, Shapiro ME, Finberg RW, Zalesnik DF, Kasper DL. Use of a model of intraabdominal sepsis for studies of the pathogenicity of *Bacteroides fragilis*. Rev Infect Dis 1984;6:591-595.

14. Kasper DL, Lindberg AA, Weintraub A, Onderdonk AB, Lonngren J. Capsular polysaccharides and lipopolysaccharides from two strains of *Bacteroides fragilis*. Rev Infect Dis 1984;6:525-529.

15. Onderdonk AB. Experimental models for inflammatory bowel disease. In: Developments in Gastroenterology, Vol 3, 1985.

16. Onderdonk AB. The carrageenan model for experimental ulcerative colitis. In: Alan R. Liss, Editor. Carcinoma of the Large Bowel and its Precursors. 1985. p. 237-245.

17. Onderdonk AB. Experimental models for ulcerative colitis. Digestive Dis Sci 1985;30:40S-44S.

18. Onderdonk AB. Role of the hamster model of antibiotic-associated colitis in defining the etiology of the disease. In: Rolfe RA, Finegold SM editors. Clostridium Difficile: It's Role in Intestinal Disease. New York, Academic Press;1988. p.115-125

19. Onderdonk AB, Delaney ML, Zamarchi GR, Hirsh ML, Munoz A, Kass EH. Normal vaginal microflora during the use of various forms of catamenial protection. Rev Infect Dis 1989;11:S61-S67.

20. Onderdonk AB. Use of an animal model system for assessing antimicrobial activity. Antimicrob Newslett 7:No. 2, Feb. 1990.

21. Onderdonk AB, Finberg RF, Kasper DL, Cisneros RL. Animal models for studying virulence of and host response to *Bacteroides fragilis*. Rev Infect Dis 1990;12:S167-177.

22. Crabb JH, Finberg R, Onderdonk AB, Kasper DL. T cell regulation of *Bacteroides fragilis*-induced intraabdominal abscesses. Rev Infect Dis 1990;12:S157-S160.

23. McDonough P, Onderdonk AB. Veterinary clinical microbiology: Parts I & II. Clin Micro Newsletter, Oct. 15, 1990 - Nov. 1, 1990, Vol. 12, Nos. 20 & 21.

24. Onderdonk AB. Comparison of in vivo methods for determining antimicrobial efficacy. editorial, Rev Infect Dis Oct-Nov. 1991

25. Onderdonk AB. Editorial response to Brook: Comparison of in vivo methods for determination of antimicrobial efficacy. Rev Infect Dis 1991;13:1181-1183.

26. Onderdonk AB, Wissemann K. Microflora of the vagina. In: Elsner J, Martius J, editors. Vulvovaginitis. New York, Marcel Dekker, Inc.;1991. p.285-304.

27. Jamas S, Easson Jr. DD, Ostroff GR, Onderdonk AB. A novel class of macrophage activating immunomodulators. In: Dunn RL, Ottenbrite PM, editors. Polmeric Drugs and Drug Delivery Systems . New York, American Chemical Society; 1991. p. 44-51.

28. Onderdonk AB. Methods for the isolation and identification of obligate anaerobes. Eur J Clin Microbiol Infect Dis 1992;11:1039-1043.

29. Onderdonk AB. Editorial Comment: CLIA '88 Better regulations or boondoggle? Infect Dis Clin Pract 1993;230-231.

30. . Onderdonk AB. Laboratory diagnosis of infectious diseases. In:Braunwald E, Wilson JD, Martin JB, Fauci AS, Kasper DL, editors. Harrison's Principles of Internal Medicine. Boston: Health Professions Divisions, McGraw-Hill Inc.; 1993. P. 489-494.

31. Onderdonk AB. Use of an animal model system for assessing the efficacy of antibiotics in treating mixed infections. Infect Dis Clin Pract 1994;S28-S33.

32. Tzianabos AO, Onderdonk AB, Kasper DL. Bacterial structure and function in relation to abscess formation. Infect Agents Dis 1994;3:256-265.

33. Becker JM, Becich MJ, Nash SV, Onderdonk AB, Stenson WF. Pouchitis - aetiology, pathogenesis, therapy. In: Johnstone P, ed. Inflammatory Bowel Disease-1994. Lancaster England, Kluwer Academic Publishers. 1994.

34. Onderdonk AB and Sasser M. Gas-liquid high-performance chromatographic methods for the identification of organisms. In: Murray PR,

Baroron Ej, Pfaller MA, Tenover FC, Yolken RH, editors. Manual of Clinical Microbiology. Washington, D.C. American Society for Microbiology Press; 1995. p.123-129.

35. Onderdonk AB, Allen S. Clostridium. In: Murray PR, Baroron Ej, Pfaller MA, Tenover FC, Yolken RH, editors. Manual of Clinical Microbiology, Washington, D.C. American Society for Microbiology Press; 1995. p. 574-586.

36. Tzianabos AO, Kasper DL, Onderdonk AB. Structure and function of *Bacteroides fragilis* capsular polysaccharides: Relationship to induction and prevention of abscesses. Clin Infect Dis 1995;20:S132-140.

37. Onderdonk AB. Microbiological models for IBD. In: Tygat GNJ, Bartelman JFWM, van Deventer SJH , Editors. Inflammatory Bowel Diseases. Hingham, MA Kluwer Academic Publishers; 1995. p.544-552.

38. Onderdonk AB, Cohen Z, Blair JE, Cisneros RL, Comstock L, DuBois A, and McLeod RC. Role of bacteria in ileal pouch disease. In: McLeod R , editor. Trends in Inflammatory Bowel Disease. Lancaster England, Kluwer Academic Publishers; 1997.

39. Tzianabos AO, Kasper DL, Cisneros RL, Smith RS, Onderdonk AB. Protection against experimental intraabdominal abscess formation. In: A.R. Eley and K.W. Bennett (eds), Anaerobic Pathogens, 1997: Sheffield Academic Press (Sheffield, England), p. 3-17.

40. Onderdonk AB. Laboratory diagnosis of infectious diseases. In: Fauci AS, Braunwald E, Isselbacher KJ ,Wilson JD, Martin JB, Kasper DL, Hauser SL, Longo DL, editors. Harrison's Principals of Internal Medicine. Boston: Health Professions Divisions, McGraw-Hill Inc. ;1998. p. 754-758.

41. Onderdonk AB, Kennedy RC. Use of animals for vaccine development. In: Paoletti LC, McInnes PM, editors. Vaccines from Concept to Clinic. Boston. CRC Press; 1998. p. 19-42.

42. Onderdonk AB. Intestinal microflora and inflammatory bowel disease. In: Kirsner JB, editor. Inflammatory Bowel Disease. Philadelphia. W.B. Saunders Company ;1999. P. 144-151.

43. Onderdonk AB, Gibson FC III, Tzianabos AO, Kasper DL. Protection against abscess formation in a model for intraabdominal sepsis. Kluwer Academic Press. Sepsis 1999; 4:311-315.

Non-print materials:

1. 1986 The Melpromene Report. The Role of the Vaginal Microflora in Toxic Shock Syndrome: What Do We Really Know?

2. 1989 Guest Interview, Lyme Disease, NBC Today Show

Patents:

1. Tzianabos AO, Onderdonk AB, Kasper DL, inventors. Capsular polysaccharide immunomodulator. US patent 5,700,787. 1997 Dec 23.

2. Tzianabos AO, Onderdonk AB, Kasper DL, inventors. Capsular polysaccharide immunomodulator. US patent 05679654. 1997 Oct 21.

3. Tzianabos AO, Onderdonk AB, Wang Y, Kasper DL, inventors; Immunomodulating Polymers. US Patent (pending)

4. Onderdonk AB ,Tzianabos AO, Miller R, Calias P, inventors; Immunomodulatory Compositions and Methods of Use Thereof . US Patent (pending)

Abstracts:

1. Onderdonk AB, Delaney ML. Assessment of the vaginal microflora during the use of various catemenial products. European Conference on Toxic Shock Syndrome, London; A2, 1997.

2. Ross RA, Fay CM, DuBois AM, Onderdonk AB. Effect of oxygen on toxic shock syndrome toxin-1 production by *Staphyloccus aureus* grown in continuous culture. European Conference on Toxic Shock Syndrome. London; A17, 1997.

3. Delaney ML, Onderdonk AB. Effect of various fiber finishes on vaginal microflora. European Conference on Toxic Shock Syndrome. London; P7, 1997.

4. Keegan S, Onderdonk AB. Evaluation of the Identicult-Albicans system. American Society for Microbiology, Annual Meeting. Atlanta;1998.

5. Sebastienelli A, Mastrantonio P, Onderdonk AB. 36kDa surface protein of *Clostridium difficile* induces cytokine response (IL-6) in intestinal cell lines. American Society for Microbiology, Annual Meeting. Atlanta; 1998.

6. Fay CL, Ross RA, Onderdonk AB. Evaluation of *Clostridium diffcile* toxin A and B using antibiotics in a continuous culture system. American Society for Microbiology, Annual Meeting. Atlanta; 1998.

7. Cisneros RL, Lawlor MS, Onderdonk AB. Colonization of the GI tract of Wistar rats by Vancomycin Resistant Enterococci (VRE). 2nd World Congress on Anaerobic Bacteria and Infections. Nice, France; 1998.

8. Delaney ML, Tzianabos AO, Onderdonk AB. Use of the Aromascan™ for detection of anaerobic bacteria. 2nd World Congress on Anaerobic Bacteria and Infections. Nice, France; 1998.

9. Lee MT-L, DuBois AM, Ross RA, Onderdonk AB. Non-linear models for in vitro kill kinetics of antibiotics. 2nd World Congress on Anaerobic Bacteria and Infections. Nice, France; 1998.

10. Seymour J, Parsonnet J, Hansmann M, DuBois A, Osterling W, Delaney M, Lawlor M, Modern P, Wieland-Alter W, Wild J, Onderdonk A. Colonization and distribution of S. aureus and TSST-1 producing S. aureus in north american women. ISSSI June 14-17, 2000

11. Seymour J, Hansmann M, Parsonnet J, Onderdonk A. Prevelance of Toxic Shock syndrome Toxin 1-producing Strains of Staphylococcus aureus and the presence of antibodies to TSST-1 in menstruating women. IIDSOG May 2002

Applicant : Alice A. Jacobs et al. Art Unit : 1637
Serial No. : 09/996,056 Examiner : Jeffrey Siew
Filed : November 27, 2001
Title : CLINICALLY INTELLIGENT DIAGNOSTIC DEVICES AND METHODS

PROPOSED CLAIMS AS OF JANUARY 7, 2005

1. (Currently amended): A method of determining a cause of one or more medical symptoms exhibited by a subject, the method comprising:

(a) obtaining one or more ~~a~~ biological samples from the subject;

(b) obtaining an array of different probes or different sets of probes, wherein each probe or set of probes selectively interacts with a target associated with a different known cause of the one or more medical symptoms, and wherein the array includes at least

(i) a first probe or set of first probes directed to a first target, wherein the first target comprises one or more markers for one or more infectious agents known to cause the one or more medical symptoms; and

(ii) a second probe or set of second probes directed to a second target, wherein the second target comprises one or more genetic markers of the subject or one or more biological or chemical molecules, all known to be a cause of the one or more medical symptoms;

(c) applying the one or more biological samples to the probes in the array under conditions that enable all of the probes to selectively interact with any targets in the biological sample;

(d) detecting interactions; and

(e) analyzing interactions to determine a cause of the one or more medical symptoms.

2. (Original): The method of claim 1, wherein the array of probes or sets of probes is arranged on a planar substrate.

3. (Original): The method of claim 1, wherein each target is a nucleic acid, peptide, polypeptide, protein, antibody, antigen, small organic molecule, inorganic molecule, enzyme, or polysaccharide.

4. (Original): The method of claim 1, wherein the array of probes comprises nucleic acid probes and polypeptide probes.

5. (Original): The method of claim 1, wherein all of the probes in the array are polypeptides.

6. (Original): The method of claim 5, wherein the probes are antibodies, antigens, enzymes, zinc-finger binding proteins, minor-groove binders, transcriptional factors, combinations thereof, or chimeras thereof.

7. (Original): The method of claim 1, wherein the subject is a plant or animal.

8. (Original): The method of claim 1, wherein the subject is a human.

9. (Original): The method of claim 1, wherein the subject is deceased.

10. (Currently amended): The method of claim 1, wherein the array includes four or more different probes or sets of probes, wherein each probe or set of probes is directed to a different target, and wherein the different first and second targets comprise at least a marker for a virus, a marker for a bacteria, a biological molecule, and a genetic marker of the subject.

11. (Original): The method of claim 1, wherein the biological sample is a blood, cerebrospinal fluid, cell culture, urine, sweat, buccal swab, tissue biopsy, or aspiration sample.

12. (Original): The method of claim 2, wherein the probes are attached to the substrate using covalent or non-covalent bonds.

13. (Original): The method of claim 2, wherein the probes are attached to the substrate using amide or thiol bonds.

14. (Original): The method of claim 1, wherein the probes are expressed on the surface of genetically modified cells.

15. (Original): The method of claim 1, wherein a probe selectively interacts with a target by specifically binding to the target to form a complex.

16. (Original): The method of claim 1, wherein a first probe selectively interacts with a target associated with an infectious disease caused by a bacteria, virus, or fungus, and a second, different probe selectively interacts with a target associated with a genetic cause.

17. (Currently amended): The method of claim 1, wherein the array of probes further comprises probes that assay for the absence of a causative agent of one or more medical symptoms.

18 and 19. (Canceled)

20. (Original): A method of claim 1, wherein all of the probes selectively interact with their respective targets under the same conditions.

21. (Canceled):

22. (Currently amended): The method of claim 49, wherein the therapeutic optimization factor is tolerance, intolerance, or susceptibility of the subject or an infectious agent to a specific drug.

23. (Currently amended): The method of claim 49, wherein the marker for the therapeutic optimization factor is a gene in a pathogen that causes susceptibility, resistance, or an idiosyncratic reaction of the pathogen when exposed to a therapeutic agent.

24 to 34. (Cancelled)

35 to 39. (Withdrawn)

40. (Canceled)

41. (Previously Presented): The method of claim 1, wherein the array of probes comprises nucleic acid probes.

42. (New): The method of claim 1, wherein all of the probes in the array are nucleic acid probes.

43. (New) The method of claim 1, wherein the array further comprises a third probe or set of third probes directed to a third target, wherein the third target comprises a marker for a therapeutic optimization factor of the subject, a marker for a therapeutic optimization factor of the first target, or both.

44. (New) The method of claim 1, wherein the biological or chemical molecule is a cancer marker, vascular marker, inflammatory marker, endocrine marker, metabolic marker, or autoimmune marker.

45. (New) The method of claim 1, wherein the biological or chemical molecule is an immunoglobulin, self-antigen, or antigen.

46. (New) The method of claim 1, wherein the biological or chemical molecule is a poison, drug, or a small organic or inorganic molecule.

47. (New) The method of claim 1, wherein the infectious agent is a virus, bacteria, fungus, or pathogenic plant.

48. (New) The method of claim 1, further comprising determining the susceptibility of the subject to a cause of the one or more medical symptoms; wherein the array further includes a third probe or set of third probes directed to a third target, wherein the third target comprises one

or more genetic markers or proteins associated with the susceptibility of the subject to a cause of the one or more medical symptoms; and wherein analyzing further comprises analyzing interactions to determine the susceptibility of the subject to a cause of the one or more medical symptoms.

49. (New) The method of claim 1, further comprising assessing the suitability of one or more therapeutic agents to treat the cause of the one or more medical symptoms; wherein the array further includes a third probe or set of third probes directed to a third target, wherein the third target comprises one or more markers for one or more therapeutic optimization factors; and wherein analyzing further comprises analyzing interactions to determine the suitability of a therapeutic agent to treat a cause of the one or more symptoms.

50. (New) The method of claim 49, wherein the third target comprises one or more markers for one or more therapeutic optimization factors for (i) two or more of the first target, (ii) two or more of the second target, or (iii) one or more of each of the first and second targets.

51. (New) The method of claim 48, further comprising assessing the suitability of one or more therapeutic agents to treat the cause of the one or more medical symptoms; wherein the array further includes a fourth probe or set of fourth probes directed to a fourth target, wherein the fourth target comprises one or more markers for one or more therapeutic optimization factors; and wherein analyzing further comprises analyzing interactions to determine the suitability of a therapeutic agent to treat a cause of the one or more symptoms.